



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,346	10/11/2003	Keun Ho Chun	58248-CIP2 (47606)	9221
7590 JHK Law P. O. Box 1078 La Canada, CA 91012-1078	05/26/2009		EXAMINER SALMON, KATHERINE D	
		ART UNIT 1634	PAPER NUMBER	
		MAIL DATE 05/26/2009	DELIVERY MODE PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/684,346	CHUN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 05 February 2009.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-9, 58-61, 82-91, 106-108, 117, 131-135, 157-159 and 228-235 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-9, 58-61, 82-91, 106-108, 117, 131-135, 157-159, 228-235 is/are rejected.
- 7) Claim(s) 231 and 234 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/27/08 entry 1 and 2</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. This action is in response to papers filed on 2/05/2009.
2. Claims 1-9, 58-61, 82-91, 106-108, 117, 131-135, 157-159, 228-235 are pending. Claims 10-57, 62-81, 92-105, 109-116, 118-132, 136-156, 160-227 have been cancelled.
3. The following rejections are newly applied as necessitated by amendment. It is noted that the art cited has previously been made of record, however, the rejections have been altered to incorporate the discussion of the new amendments to the claims. Response to arguments follows.
4. This action is FINAL.

***Noncompliance***

5. It is noted that the previous amendment to the claims was submitted on 10/27/2008 and not 10/28/2008 as stated in the notice of noncompliance (2/02/2009) (reply remarks p. 12 1<sup>st</sup> paragraph).

***Information Disclosure Statement***

6. The applicant has submitted two IDS statements (10/27/2008). These two IDS statements have been considered by the examiner.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-9, 58-61, 82-91, 106-108, 117, 131-135, 157-159, and 228-235 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 82-91, 106-108, 117, 131-135, 157-159, and 228-235 are rejected over the phrase “optionally” in part c of claim 1. It is unclear which parts after the term optionally are encompassed. Therefore it is not clear which limitations presented after the term are required limitations of the probe.

Claims 5-9, 58-61 and 228-235 are rejected over the phrase “optionally” in part c of claim 5. It is unclear which parts after the term optionally are encompassed. Therefore it is not clear which limitations presented after the term is required limitations of the probe.

8. Claims 230 and 233 are indefinite over the phrase “target agent is larger and located closer to the location” in lines 1-2. The metes and bounds of this claim is not clear because the claim does not limit target agent to being larger or located closer compared to any other structure. Therefore the metes and bounds of the claim are not defined as it is not clear how large or how close the target agent must be in order to encompass the claim limitations. Further, Claims 230 and 233 recites the limitation “the location” in line 2. There is insufficient antecedent basis for this limitation in the claim.

The previous claims never address the location of the target agent and as such it is not clear where “the location” would be and therefore the metes and bounds of “closer to the location” would not be determinable.

Claims 233-234 recite the limitation "the target agent" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 5 does not teach a target agent structure. It is suggested that the claim be amended to provide antecedent basis.

### **Response to Arguments**

The reply traverses the rejection. A summary of the arguments made in the reply is set forth below with response to arguments following.

The reply asserts that the claims' optional statements merely recite alternative embodiments in which the probe has or does not have at least one detectable label (p. 14 1<sup>st</sup> full paragraph).

This argument has been fully reviewed but has not been found persuasive.

The optional statement is not explicit as to which part of step c is optional. It is not clear if the optional statement just limits the presence or absence of the detectable label or if the optional statement encompasses all the wherein statements after part c. As such the claim has not been amended to clearly define which portions of the claim are optional and as such the metes and bounds of the claims have not been clearly defined.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-9, 58-61, 90-91, 106-108, 117, 131-135, 157-159, 228-229, 230-235 are rejected under 35 U.S.C. 102(b) as being anticipated by Tyagi et al. (US Patent 5925517 July 20, 1999).

With regard to Claim 1 step a, Tyagi et al. teaches a probe (Figure 1). The instant specification does not explicitly define an object sequence. Therefore the term is broadly interpreted as any sequence. Tyagi et al. teaches that the probe has two arms which are complementary to each other and form a hybridized duplex (Figure 1). One arm would be considered the first object and the other arm is complementary and would be considered a complement sequence (Figure 1). Tyagi et al. teaches a probe which the length of each arm (3 and 4 of Figure 1) can be 3-25 nucleotides in length (Column 12 lines 50-60).

The instant specification teaches that a recognition element specifically interacts with at least one target agent in the sample to be tested (p. 4 paragraph 21). Therefore the recognition agent is a particular part of the probe that interacts with the target. With regard to Claim 1b, Tyagi et al. teaches a part of the first object sequence and first complement sequence that interacts with a target (2a and 2b Figure 1 and Columns 9 lines 65-67). This region of the probe is conjugated to the first object arm and the

complementary arm via a coupling element. The instant specification does not define the term coupling element. However, the instant specification provides examples of types of coupling elements which would include nucleic acids (p. 40 lines 11-20).

Therefore the coupling element in Tyagi et al. would be considered the nucleic acids which attach the recognition element to the first object and complementary arms.

Therefore these nucleic acids (which could be considered as small as one nucleotide) would be smaller than the size of the target agent. Therefore the recognition element is conjugated through a coupling element to a region inside the first hybridized duplex of the region of the first object or first complement sequence which branches out (e.g. its the loop between the two hybridized arms) (figure 1 and 2).

With regard to 1c, Tyagi et al. teaches a detectable label (column 10 lines 55-65).

Tyagi et al. teaches that in the presence of a target, the recognition element is altered such that there is a signal (Column 10 lines 5-25).

With regard to Claim 2, Tyagi et al. teaches a probe in which there is a second object and a second complement sequences in the form of a target (Figure 2). Tyagi et al. teaches that a part of the target (considered an object) will bind to the complement region of the probe arm (considered a complement). This region (2b) is not the same region as the first complement (3) (Figure 2, and Figure 1). Tyagi et al. teaches that a part of the target (considered a complement) will bind to the object region of the probe arm (considered an object). This region (2a) is not the same region as the first object (4) (Figures 1 and 2). Tyagi et al. teaches a probe which the length of each arm (3 and 4 of Figure 1) can be 3-25 nucleotides in length (Column 12 lines 50-60). Tyagi et al.

teaches that in the presence of the target there is a decreased amount of the first hybridized duplex and an increase in the second hybridize duple (on and off confirmation) (Figures 1 and 2 and Column 10 lines 5-40).

With regard to Claim 3, Tyagi et al. teaches the recognition element (2 in Figure 1) is conjugated to the first object sequence (figure 1).

With regard to Claim 4, Tyagi et al. teaches the object and the complement are DNA, RNA, or a combination of DNA and RNA (column 8 lines 65-66).

With regard to Claim 5, Tyagi et al. teaches an affinity probe (Figure 1 and Column 10 lines 25-40). Tyagi et al. teaches that the probe has two arm which are complementary to each other and form a hybridized duplex (Figure 1). One arm would be considered the first object and the other arm is complementary and would be considered a complement sequence (Figure 1). Tyagi et al. teaches a probe ligand which interacts with the receptor agent (e.g. the target) (Column 17 lines 65-68 and Column 18 lines 1-25). Tyagi et al. teaches a probe which the length of each arm (3 and 4 of Figure 1) can be 3-25 nucleotides in length (Column 12 lines 50-60). Tyagi et al. teaches that the coupling element can be a 6 carbon long spacer (column 18 lines 10-15). Therefore in this example the receptor agent would be considered the target and as the target is larger than 6 carbons the coupling element is smaller than the receptor agent.

With regard to Claim 6, Tyagi et al. teaches the melting temperature of the duplex decreases by at least 10°C when hybridized (column 13 lines 1-9).

With regard to Claims 7 and 8, Tyagi et al. teaches a probe ligand coupled covalently by chemical bonds (Column 17 lines 65-68 and Column 18 lines 1-25).

With regard to Claim 9, Tyagi et al. teaches the use of chemical ligands (Column 17 lines 65-68 and Column 18 lines 1-25).

With regard to Claim 58, Tyagi et al. teaches an affinity probe which the first hybridization duplex is formed in the absence of the receptor agent (e.g. target) (Column 10 lines 5-10).

With regard to Claim 59, Tyagi et al. teaches the melting temperature of the first hybridized duplex is at least 10°C when the target is not present (column 13 lines 1-9).

With regard to Claim 60, Tyagi et al. teaches an affinity probe wherein the second hybridized duplex is preferentially formed in the presence of a target (e.g. and excess) (column 10 lines 1-24).

With regard to Claim 61, Tyagi et al. teaches the melting temperature of the duplex decreases by at least 10°C when hybridized (e.g. when in presence of an excess of target) (column 13 lines 1-9).

With regard to Claims 90 and 91, Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6).

It is noted that Claims 106 and 107 are identical in limitations except the arm sequence in 106 is liked to the 5' terminus of the first object whereas the arm sequence in 107 is linked to the first complement sequence. The terms "first object sequence" and "first complement sequence" have not been fully defined as such they encompass

any nucleic acid strands which are complementary. With regard to Claims 106 and 107, Takagi et al teaches arm sequences which are covalently linked to the first object sequence or the complement sequence at the 5' or 3' end (Figure 3, 34 and 35). It is noted that this is the same structure which is described as the arm sequence of the instant specifications Figure 20 wherein in Figure 20 8a and 8b are the arm sequences.

With regard to Claim 108, the claim is drawn to the limitations of Claims 106 and 107 wherein two of these structures are hybridized together. Takagi et al. teaches a probe that is bimolecular, wherein each molecule has the structure and are hybridizable together in a closed confirmation state (column 5 lines 9-20). Takagi et al discloses the arms are between about 3 and about 35 (Figure 3). Therefore, Takagi et al. teaches the limitations of the probe as claimed by Claim 108.

With regard to Claim 117, Tyagi et al. teaches a detectable label such as a fluorescer (Column 5 lines 65-66 and Column 6 lines 1-6).

With regard to Claims 131, Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6). Tyagi et al. teaches that the first moiety (quencher) is located on the first object sequence and the second moiety (fluorescer) is located on the complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20).

With regard to Claim 132, Takagi et al. teaches a probe that is bimolecular, wherein each molecule has the structure and are hybridizable together in a closed confirmation state (column 5 lines 9-20). Therefore there will be two molecules

hybridized that are identical. Therefore Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6). Tyagi et al. teaches that the first moiety (quencher) is located on the first object sequence and the second moiety (fluorescer) is located on the complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20). On the second molecule will be a third moiety (quencher) is located on the second object sequence and the fourth moiety (fluorescer) is located on the second complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20).

With regard to Claims 134, Tyagi et al. teaches that the first and third label are the same (quenchers).

With regard to Claim 135, Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6).

It is noted that Claims 157 and 158 are identical in limitations except the arm sequence in 106 is liked to the 5' terminus of the first object whereas the arm sequence in 107 is linked to the first complement sequence. The terms "first object sequence" and "first complement sequence" have not been fully defined as such they encompass any nucleic acid strands which are complementary.

With regard to Claims 157 and 158, Takagi et al teaches arm sequences which are covalently liked to the first object sequence or the complement sequence at the 5' or

3' end (Figure 3, 34 and 35). It is noted that this is the same structure which is described as the arm sequence of the instant specifications Figure 20 wherein in Figure 20 8a and 8b are the arm sequences. Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6). Tyagi et al. teaches that the first moiety (quencher) is located on the first object sequence and the second moiety (fluorescer) is located on the complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20).

With regard to Claim 159, the claim is drawn to the limitations of Claims 106 and 107 wherein two of these structures are hybridized together. Takagi et al. teaches a probe that is bimolecular, wherein each molecule has the structure and are hybridizable together in a closed confirmation state (column 5 lines 9-20). Takagi et al discloses the arms are between about 3 and about 35 (Figure 3). Therefore, Takagi et al. teaches the limitations of the probe as claimed by Claim 159. Takagi et al. teaches a probe that is bimolecular, wherein each molecule has the structure and are hybridizable together in a closed confirmation state (column 5 lines 9-20). Therefore there will be two molecules hybridized that are identical. Therefore Tyagi et al. teaches FRET (quencher and fluorescer) attached to the probe) to detect change in fluorescence (Column 5 lines 65-66 and Column 6 lines 1-6). Tyagi et al. teaches that the first moiety (quencher) is located on the first object sequence and the second moiety (fluorescer) is located on the complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20). On the second molecule will

be a third moiety (quencher) is located on the second object sequence and the fourth moiety (fluorescer) is located on the second complement sequence which interacts when the hybridized duplex is formed (figure 1 6, 7 and Column 10 lines 66-67 and Column 11 lines 1-20).

With regard to Claim 228, Tyagi et al. teaches a probe with the same structures as required by Claim 1 and as such teach a target detection system. It is noted that the term “system” is not defined in the instant specification. This term can broadly be interpreted as a method or a product, however, since all that is required is a product the claim is being interpreted by the examiner as a product claim.

With regard to Claim 229, Tyagi et al. teaches an example of a biotin labeled probe which would be considered a probe ligand (column 22 lines 15-30).

With regard to Claim 230 and 233, as stated in the 35 USC 112/2<sup>nd</sup> paragraph provided above, the instant claims are unclear as to how large or how close the target agent must be and therefore any target agent would broadly encompass the teaching of the claim.

With regard to Claims 232 and 235, Takagi et al. teaches a coupling agent with 3 nucleotides in length (with regard to claim 1) or one to 6 carbons in length (with regard to Claim 5). As both of these structures have a lengths less than 100nm.

With regard to claims 231 and 234, the claims are directed to probes. The structures described do not require that there be a target agent because Claim 1 merely requires the probe to comprise one operable linked component and as such does not require target agents. Further, Claim 5 does not require a target agent and as such the

target agent size does not limit the probe claimed. Therefore Tyagi et al. teaches all required structures for the claimed probe.

### **Response to arguments**

The reply traverses the rejection. A summary of the arguments set forth in the reply is provided below with response to arguments following.

The reply asserts that Tyagi et al. does not refer to a probe ligand but rather label moieties (p. 14 5<sup>th</sup> paragraph). The reply asserts that Tyagi et al. does not teach a coupling element or that the recognition element is branched out from the first hybridized duplex (p. 14 last paragraph- p. 15 1<sup>st</sup> full paragraph). The reply asserts that the claim further points out that the coupling element is essentially the same size or shorter than the size of the target agent.

These arguments have been fully reviewed but have not been found persuasive.

It is first noted that Claim 1 only requires a probe which comprises at least one of the operably linked components (see line 1-2 of the claim). As such claim 1 does not require that the probe have all three operable linked components. The claim merely requires one of the following a first pair, a recognition element, or a detectable label.

The probe ligand has not been explicitly defined by the instant specification. Tyagi et al. teaches a probe ligand which interacts with the receptor agent (e.g. the target) (Column 17 lines 65-68 and Column 18 lines 1-25). Tyagi et al. teaches a probe which the length of each arm (3 and 4 of Figure 1) can be 3-25 nucleotides in length (Column 12 lines 50-60). Tyagi et al. teaches that the coupling element to the ligand

can be a 6 carbon long spacer (column 18 lines 10-15). Therefore in this example the receptor agent would be considered the target and as the target is larger than 6 carbons (e.g. it is composed of a large nucleotide sequence) the coupling element is smaller than the receptor agent. The instant specification has not defined probe ligand. A ligand is a substance that is able to bind to and form a complex with a biomolecule. Therefore the labels taught by Tyagi et al. would be considered probe ligands. Further it is noted that claim 229 is limited to the probe ligand being a label (e.g. biotin), therefore it is clear that the term could be limited to label structures.

It is noted that the limitation for a recognition element to be branched is in the optional structure of c and therefore does not specifically limit the claimed structure. Further as discussed above Tyagi et al. teaches coupling elements which are shorter than the size of the target agent and receptor agent (see discussion about with regard to Claim 1 and 5), however, as noted the claimed structure of Claim 1 does not require this limitation to be present.

As such Tyagi et al. teaches all the required claimed elements.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 82-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. (US Patent 5925517 July 20, 1999) in view of Kolesar et al. (US Patent 6261781 July 17, 2001).

Tyagi et al. teaches a probe (Figure 1). The instant specification does not explicitly define an object sequence. Therefore the term is broadly interpreted as any sequence. Tyagi et al. teaches that the probe has two arms which are complementary to each other and form a hybridized duplex (Figure 1). One arm would be considered the first object and the other arm is complementary and would be considered a complement sequence (Figure 1). Tyagi et al. teaches a probe which the length of each arm (3 and 4 of Figure 1) can be 3-25 nucleotides in length (Column 12 lines 50-60).

The instant specification teaches that a recognition element specifically interacts with at least one target agent in the sample to be tested (p. 4 paragraph 21). Therefore

the recognition agent is a particular part of the probe that interacts with the target.

Tyagi et al. teaches a part of the first object sequence and first complement sequence that interacts with a target (2a and 2b Figure 1 and Columns 9 lines 65-67).

Tyagi et al. teaches a detectable label (column 10 lines 55-65).

Tyagi et al. teaches that in the presence of a target, the recognition element is altered such that there is a signal (Column 10 lines 5-25).

With regard to Claim 83, Tyagi et al. teaches a probe that is bimolecular, wherein each molecule has the structure and are hybridizable together in a closed confirmation state (column 5 lines 9-20), therefore the probes a first molecule and a second molecule.

With regard to Claim 84, Tyagi et al. teaches a probe wherein it is immobilized to a support (Figure 10).

With regard to Claims 85 and 89, Tyagi et al. teaches the first object and first complement are covalently linked by a loop (Figure 3).

With regard to Claims 86 and 88, Tyagi et al. teaches that the loop connects the 3' of the object to the 5' of the complement and therefore the first object, the loop, and the first complement are covalently linked in a 5' to 3' direction (Figure 3). With regard to

Claim 87, Tyagi et al. teaches a probe wherein the loop has 37 nucleotides (between 4 and 100 nucleotides) (Figure 3).

Tyagi et al. however, does not teach the detectable label on the probe structure is an intercalating dye which can preferentially bind to double-stranded nucleic acids.

With regard to Claim 82, Kolesar et al. teaches probes with a detectable label such as an intercalating dye (Column 7, lines 35-50).

Therefore it would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the probe of Tyagi et al. to have an intercalator detectable label as taught by Kolesar et al. with a reasonable expectation of success. The ordinary artisan would be motivated to modify the probe of Tyagi et al. to have an intercalator detectable label as taught by Kolesar et al. because Kolesar et al. teaches that using an intercalating dye in a duplex hybrid dramatically increases the stability of the hybrid especially for RNA-DNA hybrids (Column 7, lines 35-50). Therefore the ordinary artisan would be motivated to label with intercalating dye to increase stability.

### **Response to arguments**

The reply traverses the rejection. A summary of the reply is presented below with response to arguments following.

The reply asserts that none of the references teach a probe with a coupling element that is essentially the same size or shorter than the size of the target agent.

Although Claim 1 has been rejected by Tyagi et al. as teaching a coupling element that is essentially the same size or shorter than the size of the target agent. (see rejection of Claim 1 under 35 USC 102(b)), it is noted that Claim 1 does not require this limitation. Specifically Claim 1 is drawn to a probe comprising “at least one and preferably all of the following as operably linked components”. Therefore as long as Tyagi et al. teaches one component of the structure listed in Claim 1, Tyagi teaches all

the requirements of the claim. As such the limitation that that coupling element is essentially the same size or shorter than the size of the target agent does not limit the claimed invention.

***Conclusion***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/  
Examiner, Art Unit 1634

/Sarae Bausch/  
Primary Examiner, Art Unit 1634